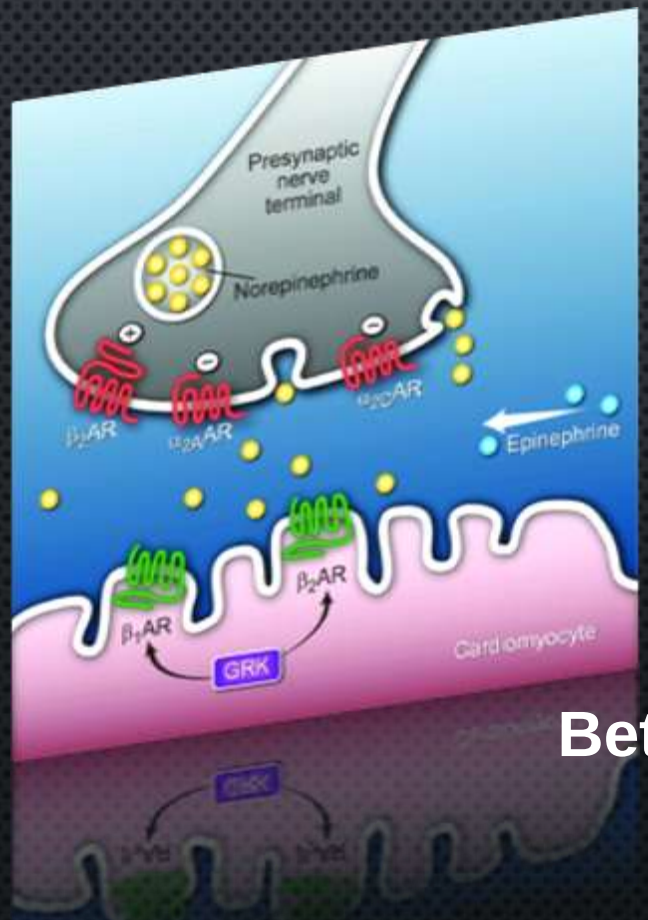
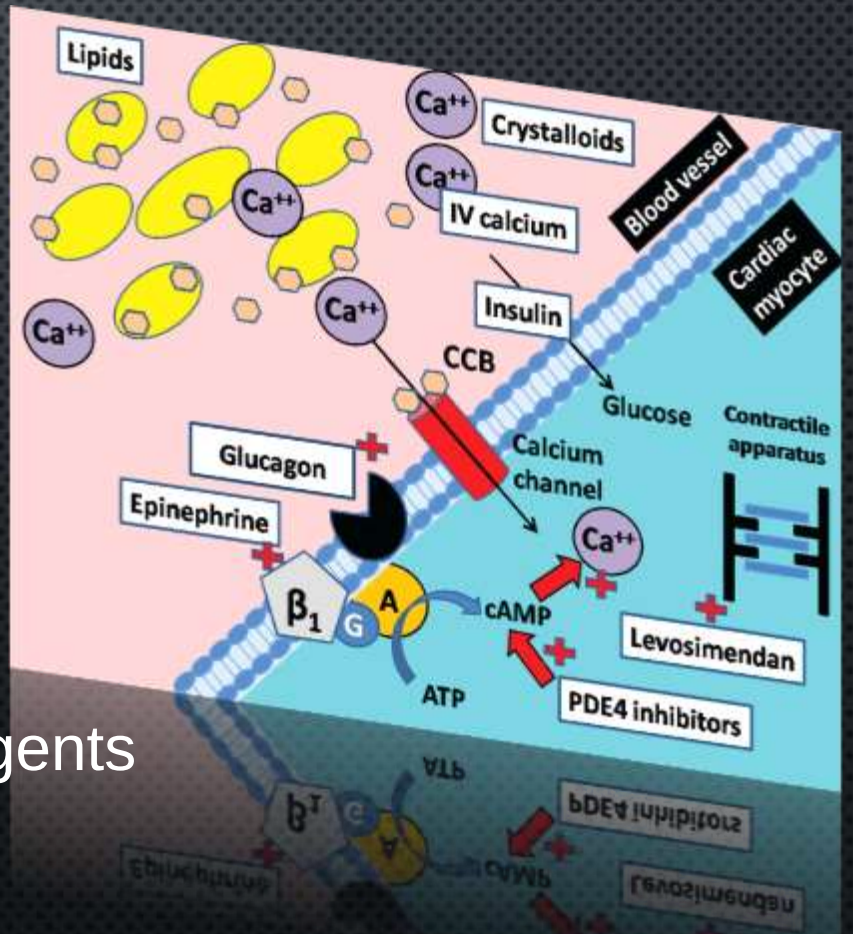
PERIOPERATIVE BETA BLOCKADE: THE CONTROVERSY CONTINUES



Central

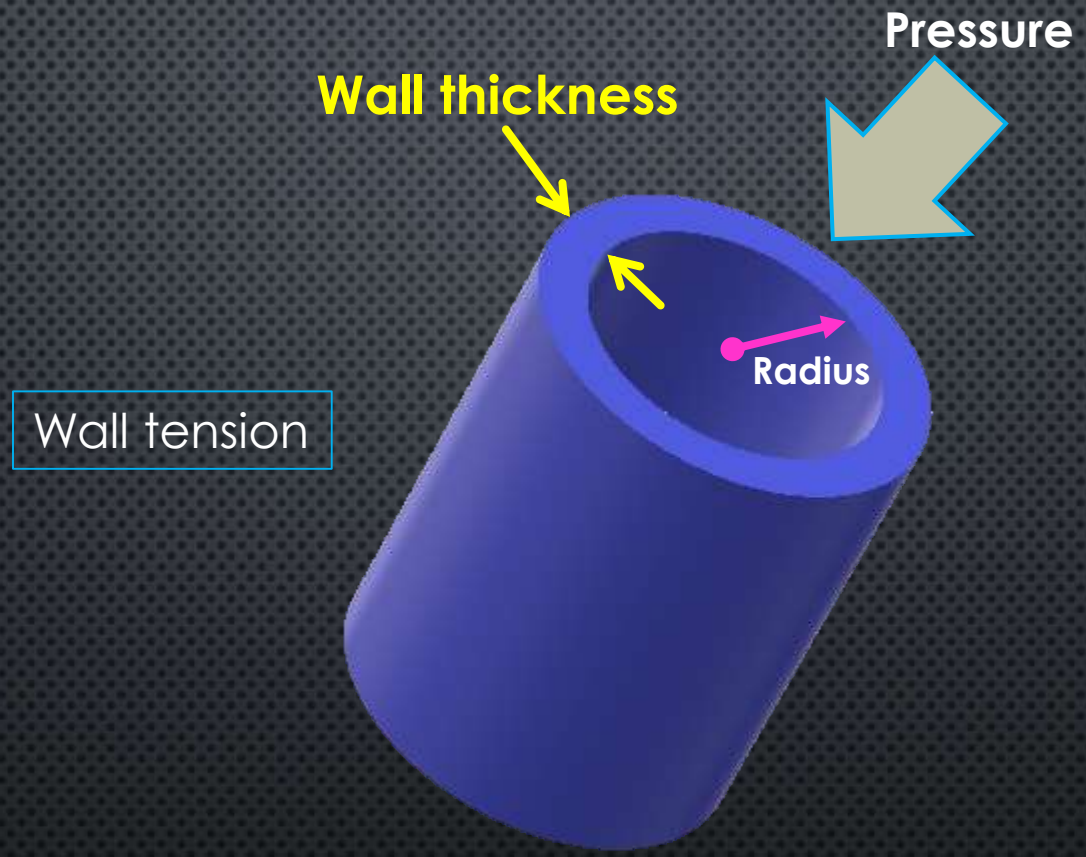
Peripheral Eye/others



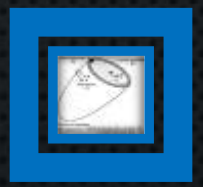
Beta-adrenergic blocking agents

Major factors in myocardial oxygen consumption

Basic physiology



Law of Laplace most often used in hemodynamics gives the relation between transmural pressure and the stress in the wall in organs with a wall thickness h.

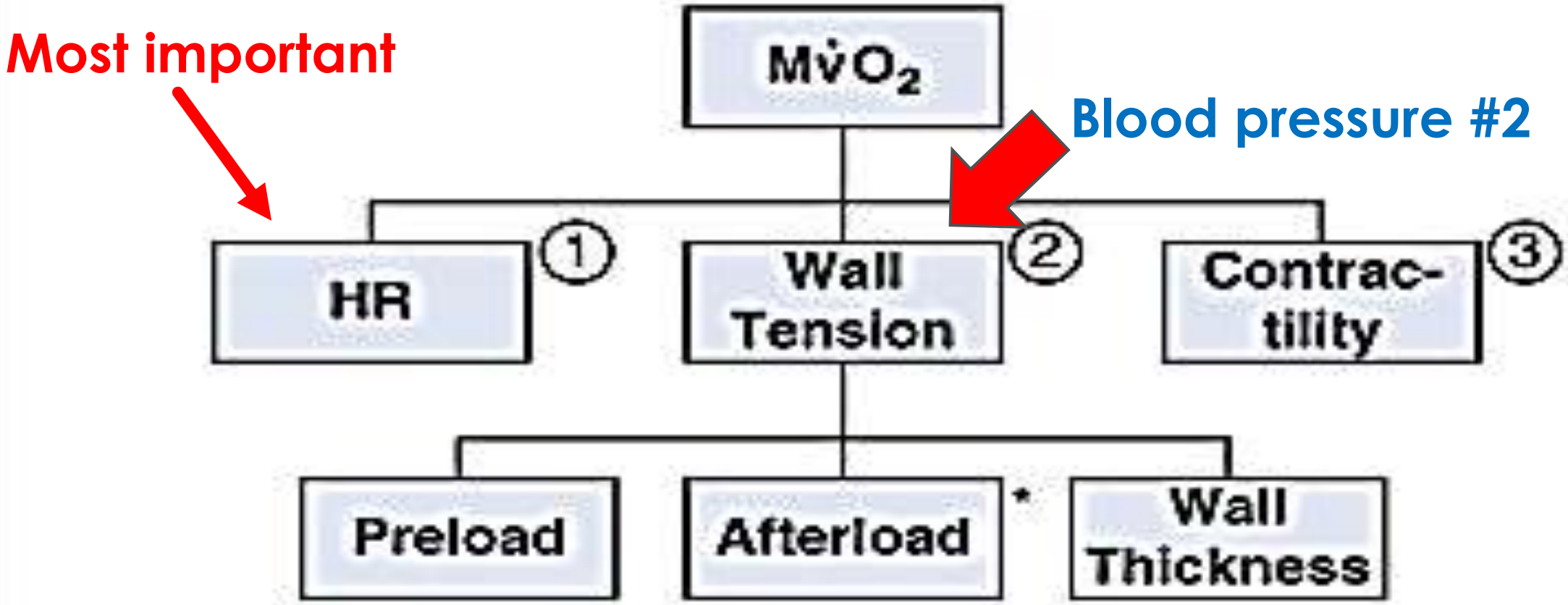


Law of Laplace

Myocardial O_2 Demand

(O_2 Consumption, $M\dot{V}O_2$)

$M\dot{V}O_2$ Normal Range = 8–15 mL O_2/min/100 gm LV



Beta blockers

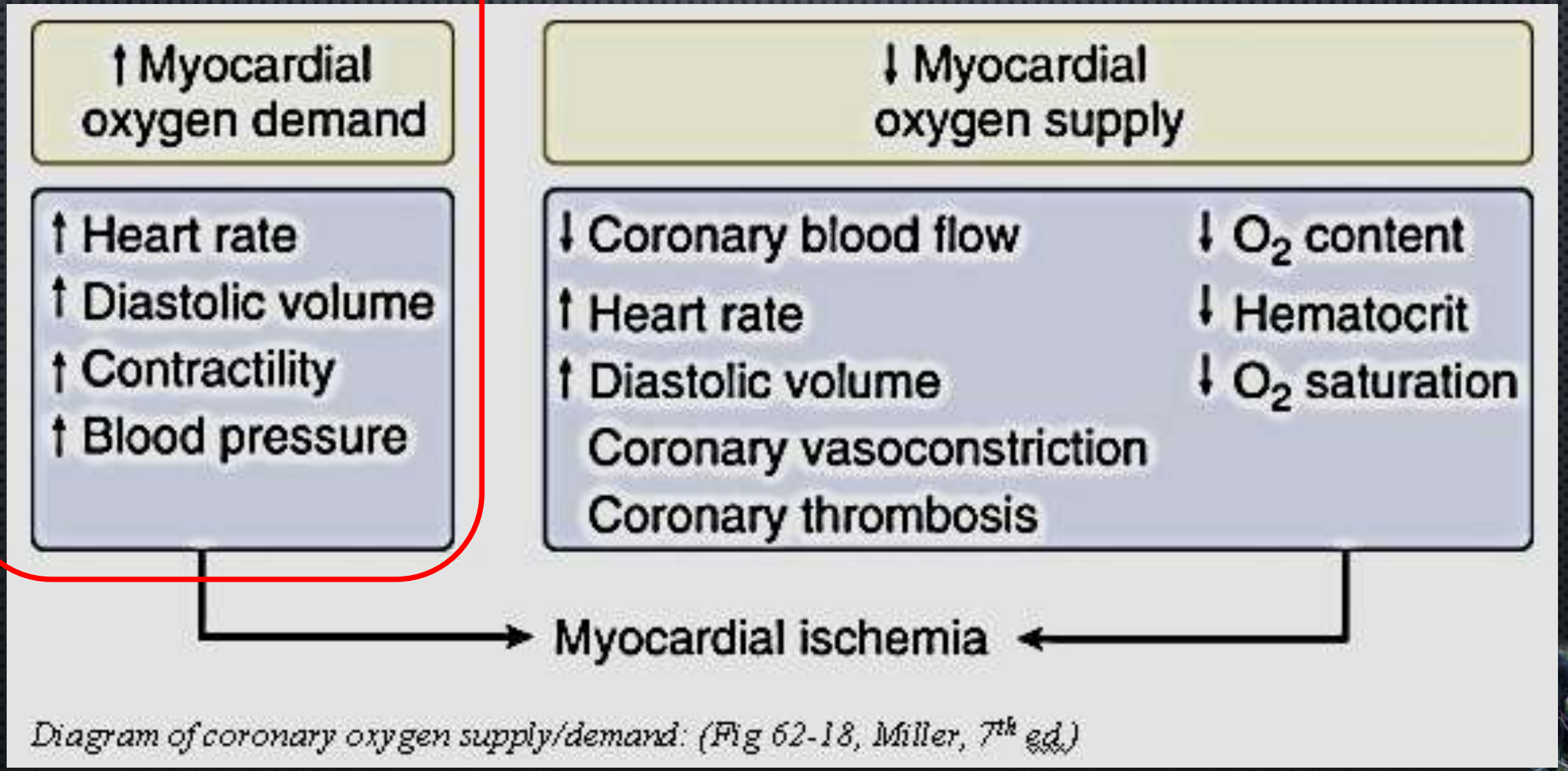
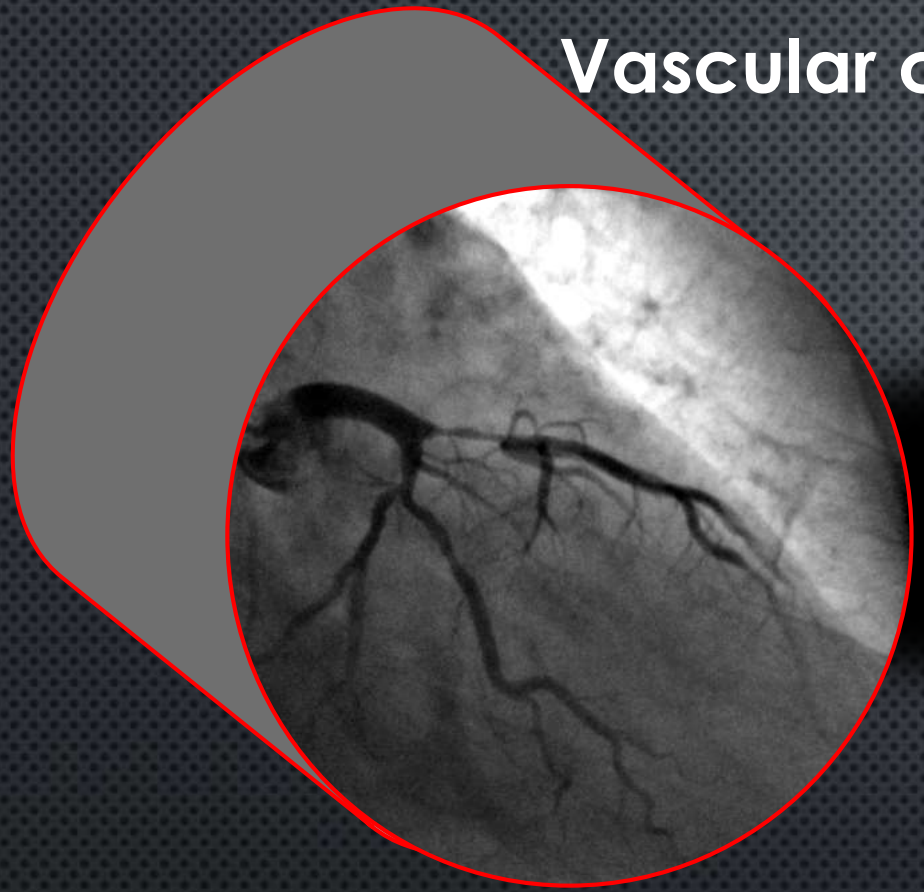


Diagram of coronary oxygen supply/demand: (Fig 62-18, Miller, 7th ed.)

Vascular concerns in atherosclerosis



CAUTION

Efferent arteriole

Diabetes kidney

Dilated afferent arteriole

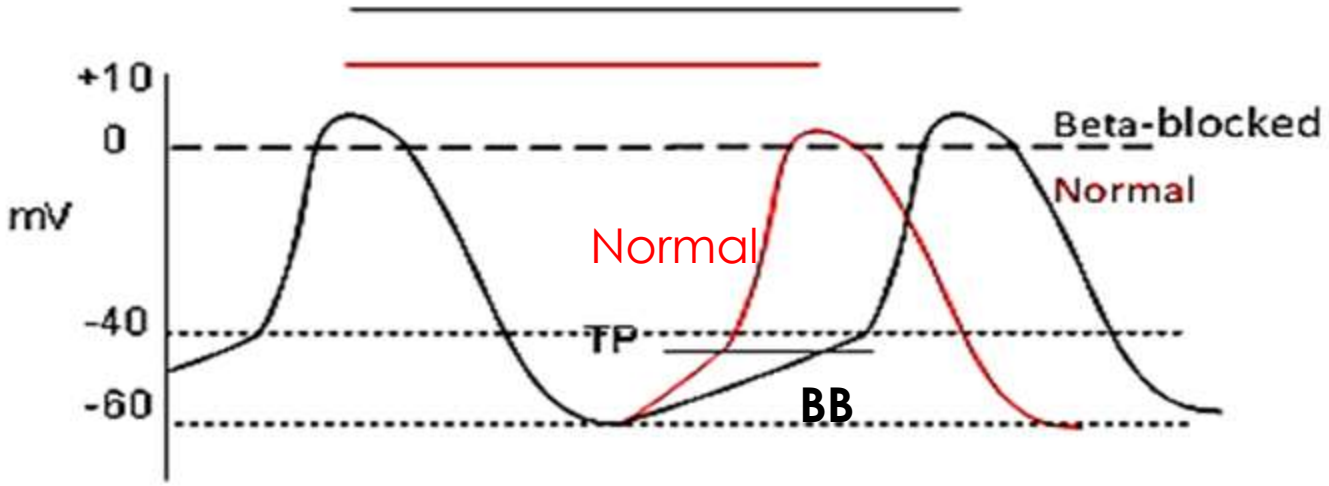
Urine/protein

SURGERY CONSIDERATIONS AND BETA BLOCKERS

- Beta blockers reduce myocardial oxygen consumption
  - Reduces demand from increased catecholamine release
  - Reduce arrhythmia's and control heart rate (most important factor in mvo2 equation)
- Acute withdrawal of beta blockers can increase mortality
  - American Heart Journal 2001:141:148
- Most commonly beta blockers are continued
- BB preoperatively is less clear and most agree not during acute heart failure
- Use of BB for heart rate control in patients with normal LV during surgery is primarily the use of esmolol (metoprolol) others

B1 selective-less problems with lungs and PVDx ???

Beta-Blockade



- Beta-blockers cause bradycardia through blockage of B_1 receptors
- This reduces levels of cAMP and intracellular calcium
- Slope of pre-potential (phase 4) is reduced
- Often cause AV conduction disturbance (increased PR interval /heart block) and bradycardia

NON CARDIAC SURGERY RECOMMENDATIONS AT PRESENT 2019

- PROPHYLACTIC BETA BLOCKERS ARE NOT RECOMMENDED TO IMPROVE PERIOPERATIVE OUTCOMES
  - INCREASE RISK OF STROKE AND DEATH

- CONTINUE BETA BLOCKERS
  - HYPERTENSION
  - ATRIAL FIBRILLATION HEART RATE CONTROL
  - ANGINA , HEART FAILURE
  - PRIOR MI

N=200

The New England
Journal of Medicine

VOLUME 335 DECEMBER 5, 1996 NUMBER 23

EFFECT OF ATENOLOL ON MORTALITY AND CARDIOVASCULAR MORBIDITY AFTER NONCARDIAC SURGERY

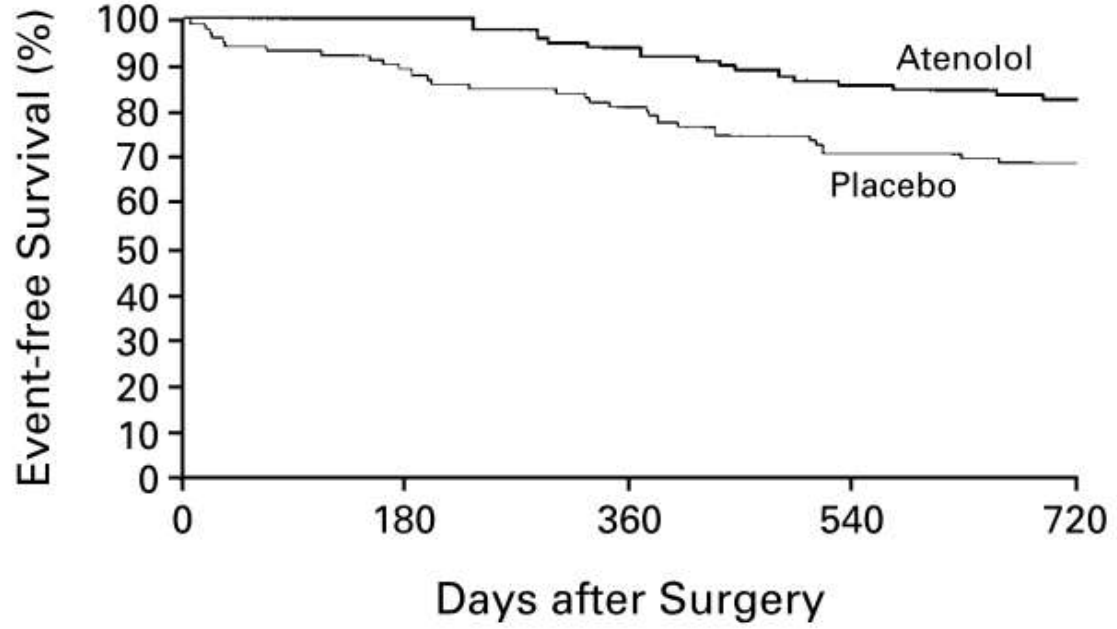
DENNIS T. MANGANO, PH.D., M.D., ELIZABETH L. LAYUG, M.D., ARTHUR WALLACE, PH.D., M.D., AND IDA TATEO, M.S., FOR THE MULTICENTER STUDY OF PERIOPERATIVE ISCHEMIA RESEARCH GROUP*

Randomized, double blind, placebo-controlled trial to compare the effect of atenolol with that of a placebo on overall survival and cardiovascular morbidity in patients with or at risk for coronary artery disease who were undergoing non-cardiac surgery.

N Engl J Med 1996;335:1713-20

Conclusions

In patients who have or are at risk for coronary artery disease who must undergo noncardiac surgery, treatment with atenolol during hospitalization can reduce mortality and the incidence of cardiovascular complications for as long as two years after surgery.



Characteristic	Atenolol (N=99)	Placebo (N=101)	P Value
Definite coronary artery disease (%)	36	42	0.38
At risk for coronary artery disease (%)†	63	59	0.38
History of cardiac disease (%)			
Myocardial infarction	18	26	0.26
Coronary bypass surgery	11	17	0.31
Percutaneous transluminal coronary angioplasty	1	3	0.30
Typical angina	25	36	0.13
Dysrhythmia	13	13	1.00
Congestive heart failure	9	7	0.61
Cardiac risk factors (%)			
Current smoking	35	38	0.77
Hypertension	71	60	0.08
Cholesterol ≥240 mg/dl (6.2 mmol/liter)	10	6	0.31
Diabetes mellitus	28	35	0.36
Age ≥65 yr	65	75	0.22

N Engl J Med 1996;335:1713-20

Cochrane Library

Cochrane Database of Systematic Reviews

88 randomized controlled trials with 19,161 participants

Perioperative beta-blockers for preventing surgery-related mortality and morbidity (Review)

Blessberger H, Kammler J, Domanovits H, Schlager O, Wildner B, Azar D, Schillinger M, Wiesbauer F, Steinwender C

2018

CARDIAC SURGERY (53 trials)

Cochrane

We found no clear evidence of an effect of beta-blockers on the following outcomes.

- All-cause mortality: RR 0.73, 95% CI 0.35 to 1.52, 3783 participants, moderate quality evidence.
- Acute myocardial infarction (AMI): RR 1.04, 95% CI 0.71 to 1.51, 3553 participants, moderate quality evidence.
- Myocardial ischaemia: RR 0.51, 95% CI 0.25 to 1.05, 166 participants, low quality evidence.
- Cerebrovascular events: RR 1.52, 95% CI 0.58 to 4.02, 1400 participants, low quality evidence.
- Hypotension: RR 1.54, 95% CI 0.67 to 3.51, 558 participants, low quality evidence.
- Bradycardia: RR 1.61, 95% CI 0.97 to 2.66, 660 participants, low quality evidence.
- Congestive heart failure: RR 0.22, 95% CI 0.04 to 1.34, 311 participants, low quality evidence

Beta-blockers significantly reduced the occurrence of the following endpoints

Cochrane

- Ventricular arrhythmias: **RR 0.37, 95% CI 0.24 to 0.58**, number needed to treat for an additional beneficial outcome (NNTB) 29, 2292 participants, moderate quality evidence.

- Supraventricular arrhythmias: **RR 0.44, 95% CI 0.36 to 0.53**, NNTB five, 6420 participants, high quality evidence.

- On average, beta-blockers **reduced length of hospital stay** by 0.54 days (95% CI -0.90 to -0.19, 2450 participants, low quality evidence).

NON-CARDIAC SURGERY (35 trials)

Cochrane

Beta-blockers significantly increased the occurrence of the following adverse events.

- **All-cause mortality: RR 1.25, 95% CI 1.00 to 1.57**, 11,413 participants, low quality of evidence, number needed to treat for an additional harmful outcome (NNTH) 167.

- **Hypotension: RR 1.50, 95% CI 1.38 to 1.64,** NNTH 16, 10,947 participants, high quality evidence.

- **Bradycardia: RR 2.23, 95% CI 1.48 to 3.36,** NNTH 21, 11,033 participants, moderate quality evidence.

We found a potential increase in the occurrence of the following outcomes with the use of beta-blockers.

Cochrane

Beta-blockers significantly reduced the occurrence of the following endpoints.

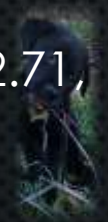
- **AMI: RR 0.73, 95% CI 0.61 to 0.87, NNTB 76, 10,958 participants, high quality evidence.**
- **Myocardial ischaemia: RR 0.51, 95% CI 0.34 to 0.77, NNTB nine, 978 participants, moderate quality evidence.**

- **Supraventricular arrhythmias: RR 0.73, 95% CI 0.57 to 0.94,** NNTB 112, 8744 participants, high quality evidence.

We found **no clear evidence of an effect of beta-blockers** on the following outcomes.

- **Ventricular arrhythmias: RR 0.68, 95% CI 0.31 to 1.49**, 476 participants, moderate quality evidence.
- **Congestive heart failure: RR 1.18, 95% CI 0.94 to 1.48**, 9173 participants, moderate quality evidence.
- Length of hospital stay: mean difference -0.45 days, 95% CI -1.75 to 0.84, 551 participants, low quality evidence.

Cerebrovascular events: RR 1.59, 95% CI 0.93 to 2.71,



CARDIAC SURGERY (53 trials)

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Beta-blockers significantly reduced the occurrence of the following endpoints.

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2292 participants, moderate quality evidence.
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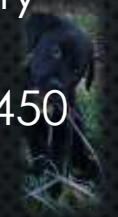

Cochrane

In non-cardiac surgery, evidence shows an association of beta-blockers with increased all-cause mortality.

Closing comments

N=4315 patients

Six independent predictors of major cardiac complications[1]
High-risk type of surgery (examples include vascular surgery and any open intraperitoneal or intrathoracic procedures)
History of ischemic heart disease (history of myocardial infarction or a positive exercise test, current complaint of chest pain considered to be secondary to myocardial ischemia, use of nitrate therapy, or ECG with pathological Q waves; do not count prior coronary revascularization procedure unless one of the other criteria for ischemic heart disease is present)
History of heart failure
History of cerebrovascular disease
Diabetes mellitus requiring treatment with insulin
Preoperative serum creatinine >2.0 mg/dL (177 micromol/L)

Circulation 1999:100:1043

Prospective cohort study
In Hospital

Rate of cardiac death, nonfatal myocardial infarction, and nonfatal cardiac arrest according to the number of predictors[2]

No risk factors – 0.4% (95% CI: 0.1-0.8)
One risk factor – 1.0% (95% CI: 0.5-1.4)
Two risk factors – 2.4% (95% CI: 1.3-3.5)
Three or more risk factors – 5.4% (95% CI: 2.8-7.9)

Circulation 1999:100:1043

Derivation and Prospective Validation of a Simple Index for Prediction of Cardiac Risk of Major Noncardiac Surgery

Thomas H. Lee, MD, SM; Edward R. Marcantonio, MD, SM; Carol M. Mangione, MD, SM; Eric J. Thomas, MD, SM; Carisi A. Polanczyk, MD; E. Francis Cook, ScD; David J. Sugarbaker, MD; Magruder C. Donaldson, MD; Robert Poss, MD; Kalon K.L. Ho, MD, SM; Lynn E. Ludwig, MS, RN; Alex Pedan, PhD; Lee Goldman, MD, MPH

Background—Cardiac complications are important causes of morbidity after noncardiac surgery. The purpose of this prospective cohort study was to develop and validate an index for risk of cardiac complications.

Methods and Results—We studied 4315 patients aged ≥50 years undergoing elective major noncardiac procedures in a tertiary-care teaching hospital. The main outcome measures were major cardiac complications. Major cardiac complications occurred in 56 (2%) of 2893 patients assigned to the derivation cohort. Six independent predictors of complications were identified and included in a Revised Cardiac Risk Index: high-risk type of surgery, history of ischemic heart disease, history of congestive heart failure, history of cerebrovascular disease, preoperative treatment with insulin, and preoperative serum creatinine >2.0 mg/dL. Rates of major cardiac complication with 0, 1, 2, or ≥3 of these factors were 0.5%, 1.3%, 4%, and 9%, respectively, in the derivation cohort and 0.4%, 0.9%, 7%, and 11%, respectively, among 1422 patients in the validation cohort. Receiver operating characteristic curve analysis in the validation cohort indicated that the diagnostic performance of the Revised Cardiac Risk Index was superior to other published risk-prediction indexes.

Conclusions—In stable patients undergoing nonurgent major noncardiac surgery, this index can identify patients at higher risk for complications. This index may be useful for identification of candidates for further risk stratification with noninvasive technologies or other management strategies, as well as low-risk patients in whom additional evaluation is unlikely to be helpful. (***Circulation.*** **1999;100:1043-1049.)**

TABLE 4. Rates of Major Cardiac Complications and Multivariate ORs* Among Patients With Individual Risk Factors in Derivation and Validation Sets

	Derivation Set (n=2893)		Validation Set (n=1422)	
	Crude Data	Adjusted OR (95% CI)	Crude Data	Adjusted OR (95% CI)
Revised Cardiac Risk Index				
1. High-risk type of surgery	27/894 (3%)	2.8 (1.6, 4.9)	18/490 (4%)	2.6 (1.3, 5.3)
2. Ischemic heart disease	34/951 (4%)	2.4 (1.3, 4.2)	26/478 (5%)	3.8 (1.7, 8.2)
3. History of congestive heart failure	23/434 (5%)	1.9 (1.1, 3.5)	19/255 (7%)	4.3 (2.1, 8.8)
4. History of cerebrovascular disease	17/291 (6%)	3.2 (1.8, 6.0)	10/140 (7%)	3.0 (1.3, 6.8)
5. Insulin therapy for diabetes	7/112 (6%)	3.0 (1.3, 7.1)	3/59 (5%)	1.0 (0.3, 3.8)
6. Preoperative serum creatinine >2.0 mg/dL	9/103 (9%)	3.0 (1.4, 6.8)	3/55 (5%)	0.9 (0.2, 3.3)

*Based on logistic regression models including these 6 variables.

Circulation 1999:100:1043

Rate of myocardial infarction, pulmonary edema, ventricular fibrillation, primary cardiac arrest, and complete heart block[1]
No risk factors – 0.5% (95% CI: 0.2-1.1)
One risk factor – 1.3% (95% CI: 0.7-2.1)
Two risk factors – 3.6% (95% CI: 2.1-5.6)
Three or more risk factors – 9.1% (95% CI: 5.5-13.8)

Circulation 1999:100:1043